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Taking Attention Out of Context: Frontopolar Transcranial Magnetic Stimulation Abolishes the Formation of New Context Memories in Visual Search

Artyom Zinchenko¹, Markus Conci¹, Paul C. J. Taylor¹,
Hermann J. Müller^{1,2}, and Thomas Geyer¹

Abstract

■ This study investigates the causal contribution of the left frontopolar cortex (FPC) to the processing of violated expectations from learned target–distractor spatial contingencies during visual search. The experiment consisted of two phases: learning and test. Participants searched for targets presented either among repeated or nonrepeated target–distractor configurations. Prior research showed that repeated encounters of identically arranged displays lead to memory about these arrays, which then can come to guide search (contextual cueing effect). The crucial manipulation was a change of the target location, in a nevertheless constant distractor layout, at the transition from learning to test. In addition to this change, we applied repetitive transcranial magnetic stimulation (rTMS) over the left lateral FPC, over a posterior control site, or no rTMS at all (baseline; between-group manipulation) to see

how FPC rTMS influences the ability of observers to adapt context-based memories acquired in the training phase. The learning phase showed expedited search in repeated relative to nonrepeated displays, with this context-based facilitation being comparable across all experimental groups. For the test phase, the recovery of cueing was critically dependent on the stimulation site: Although there was evidence of context adaptation toward the end of the experiment in the occipital and no-rTMS conditions, observers with FPC rTMS showed no evidence of relearning at all after target location changes. This finding shows that FPC plays an important role in the regulation of prediction errors in statistical context learning, thus contributing to an update of the spatial target–distractor contingencies after target position changes in learned spatial arrays. ■

INTRODUCTION

Prediction errors are key features in current accounts of perception, learning, and action. At the heart of these so-called predictive coding theories (Friston, 2010; Rao & Ballard, 1999) is the idea that the brain is essentially an inference machine that actively tries to explain its sensations. In this regard, hierarchically higher brain areas modulate (“predict”) the tuning properties of lower level areas via feedback processing. Lower level areas, in turn, compute the differences between top–down expectations and the actual sensory input, with this difference providing a prediction error signal. In this scheme, prediction errors serve as important learning signals that may cause a reevaluation and thus an update of current expectations.

In this study, we examined the contribution of the frontopolar cortex (FPC) to the regulation of prediction errors in a selective attention, that is, visual search, task. In recent years, contributions of the anterior pFC have

been shown in a variety of “easy” feature singleton and “difficult” conjunction search tasks (see Pollmann, Weidner, Müller, & von Cramon, 2006, for an overview). The critical finding in these studies is that of increased anterior pFC activations following a change of the target’s perceptual dimension (e.g., when an orientation-defined target is followed by a color-defined target) relative to a dimension repeat trial (e.g., a color target is followed by another color target). According to predictive coding theories, the enhanced prefrontal activations following dimension change trials may reflect a larger prediction error, relative to dimension repeat trials, because expectations about the target’s (repeated) dimensional identity are violated (see Summerfield, Trittschuh, Monti, Mesulam, & Egner, 2008, for the idea that BOLD signal amplitudes index top–down expectations). Furthermore, it has been suggested that the anterior pFC regulates prediction errors by attentionally weighting/amplifying the target’s perceptual dimension to determine the presence and location of the search target at an overall salience or master map of the visual array (Weidner, Pollmann, Müller, & von Cramon, 2002). Although these findings may suggest a contribution of

¹Ludwig-Maximilians-Universität München, ²Birkbeck, University of London

the pFC to predictive coding, for example, by shifting attention toward the (changed) perceptual dimension of the current target and thus increasing the efficacy of perceptual inference (e.g., Kok, Rahnev, Jehee, Lau, & de Lange, 2012), more recent studies show that the anterior pFC, besides its effects on dimension-based attention, is also involved in the control of visuospatial attention following target location changes in learned display arrangements (Pollmann & Manginelli, 2009; Pollmann et al., 2007).

Pollmann and Manginelli (2009) measured fMRI (BOLD) activations while having their observers perform a relatively difficult letter search task, divided into a learning phase and a test phase. Unbeknown to observers, in half of the trials, the target was presented within a constant spatial layout of distractor elements, enabling them to associate the target with the constant distractor configuration (see Chun & Jiang, 1998). Following initial learning, in the subsequent test phase, a change of the target position was introduced in an otherwise constant distractor array. This target location change was implemented to test whether and how context memory adapts to this change and which neuronal structures support the adaptation. Pollmann and Manginelli (2009) observed a postchange reduction of contextual cueing in terms of search RTs, accompanied by a significant increase in BOLD activations in the left FPC, in addition to various other regions of the frontoparietal attention network (Corbetta & Shulman, 2002). Although fMRI activations were initially reduced for repeated relative to nonrepeated displays, the processing of repeated (relative to nonrepeated) displays led to stronger activations after target position changes in the subsequent test phase. Importantly, the magnitude of postchange FPC activations for repeated displays was positively correlated with the strength of the contextual cueing effect in the initial learning phase, although there was no systematic relationship between postchange contextual cueing and FPC activations. Based on these findings, Pollmann and Manginelli (2009) hypothesized that FPC serves a dual function in the processing of changes in learned, contextual cueing arrays: first, to detect changes in these arrays, and second, to inform other structures of the frontoparietal network about display changes. Via the latter, FPC would effectively help make the subtle target position change more salient, thus supporting frontoparietal structures in the reallocation of attention to the changed target position. According to this view, FPC would facilitate the adaptation of contextual cueing by initiating attention shifts toward the changed target position. However, given that the adaptation process is typically not very efficient (see below), there is at least one alternative interpretation of (increased) FPC activations in the processing of changed contextual cueing displays, namely, that these activations reflect additional cognitive (executive) processes required for the suppression of the current sensory input, that is, the changed target position.

In other words, FPC would contribute to the enhanced processing of initially learned (old) distractor arrangements, rather than facilitating the processing of changed (new) target locations in these arrangements. The current study used rTMS to evaluate the two alternative accounts of FPC function in a context memory adaptation task.

FPC as Facilitator of Old or New Target Positions?

The ability to form new associations between target positions and the spatial pattern formed by the repeated distractor locations is strongly affected by already existing context memory representations (Zellin, von Mühlenen, Müller, & Conci, 2014; Zellin, Conci, von Mühlenen, & Müller, 2011, 2013; Conci & Müller, 2012; Conci, Sun, & Müller, 2011; Makovski & Jiang, 2010). Collectively, these studies show that learning of target–distractor associations is typically limited to a single target location within a given arrangement (Zellin et al., 2011) and that adaptation of contextual cueing after a target location change is rather inefficient, with a persisting attentional bias toward the old target position (Zellin et al., 2013, 2014; Conci & Müller, 2012; Conci et al., 2011; Manginelli & Pollmann, 2009). One possible reason why contextual cueing exhibits resistance to adapt to changed target locations is that context learning is resource demanding, relying on visual working memory resources (e.g., Annac et al., 2013; Jungé, Scholl, & Chun, 2007; Jiang & Leung, 2005). Thus, it may cease after a number of repeated encounters of the same arrangements, as the target–distractor relations are typically stable over time, so that there would be no additional processing advantages if resource-dependent learning were to continue. A related idea is to conceive contextual cueing as a predictive coding mechanism (e.g., Zinchenko, Conci, Müller, & Geyer, 2018; Conci, Zellin, & Müller, 2012) that takes into account the distribution or reliability of statistical signals (i.e., of repeated search arrays) in context learning. For instance, over the course of learning, observers may come to form hypotheses about regularities (or their absence) in the displays encountered, which then influence the way they process target location changes. Thus, a search scenario with only 50% repeated displays may not be experienced as a “statistically rich” sensory environment, causing observers to “turn off” further learning. In terms of perceptual inference, the turning off of learning would be equivalent to the maintenance of the already established context memory. From this perspective, subsequent to a target location change, observers may still exhibit a strong tendency to expect the target at the old, that is, learned, target position (see, e.g., Manginelli & Pollmann, 2009, or Zellin et al., 2014), accompanied by a suppression of prediction errors signaling a mismatch between the current and learned target positions.

In summary, Pollmann and Manginelli (2009) observed increased FPC activations following target location changes in learned search arrays. Although these activations may reflect prediction errors due to FPC being involved in the matching of learned predictions and sensory input, what role the FPC plays in the regulation of these errors remains an open issue. Conceivably, FPC might help minimize prediction errors by facilitating the processing of the new, that is, relocated, target position, thus supporting the (in any case slow) adaptation of context memories to the new distractor-to-target spatial relations (“FPC+” hypothesis). Alternatively, FPC might contribute to “resolving” prediction errors through suppression of the changed sensory input (“FPC–” hypothesis), as a result of which the priority assigned to the initially learned target position would tend to be maintained. In short, FPC might be involved either in reinforcing processing of the already learned target location while suppressing the changed input (FPC–) or in facilitating adaptation to a new target location in an otherwise unchanged array of distractors (FPC+).

Rationale of This Study

On this background, this study was designed to investigate the role of the FPC in the adaptation of contextual cueing. Specifically, we applied low-frequency rTMS to examine the contribution of the left FPC in the processing of repeated distractor configurations after target location changes. rTMS may reduce and/or inhibit excitability in the underlying cortex (Filipović, Rothwell, & Bhatia, 2010; Hoffman & Cavus, 2002; Wassermann & Lisanby, 2001). For this reason, we applied rTMS to FPC after an initial learning phase and before a subsequent test phase to examine its effects on context adaptation. According to the FPC– hypothesis, prediction errors are minimized by suppressing the changed target location (thus enhancing the initial target location). A transient disruption of this inhibitory process should, in turn, facilitate context adaptation, and as a result, the changed target location would be incorporated more effectively into the existing context representation. By contrast, the FPC+ hypothesis would postulate a relatively rapid adaptation, facilitating learning of the changed input. In this case, rTMS-induced interference of FPC should weaken adaptation, thus supporting the maintenance of existing target–distractor associations and impeding positional biasing toward the changed target locations. rTMS over the FPC was compared against rTMS over a control (posterior) region as well as a no-TMS baseline condition to ensure that variations of the adaptation of contextual cueing were causally linked to FPC functioning rather than being associated with non-specific effects that may have resulted from the rTMS methodology.

METHODS

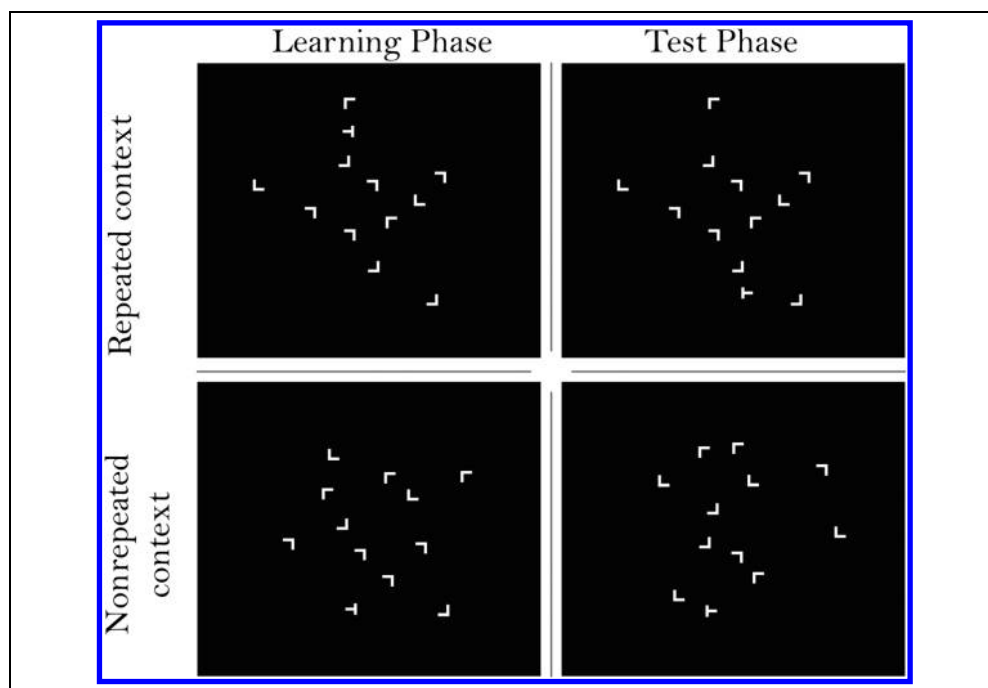
Participants

Forty-two right-handed participants naive to the purpose of the study took part in the experiment (mean age = 26.5 years, 24 women). The sample size was determined on the basis of previous contextual cueing studies (e.g., Zellin et al., 2013; Geyer, Zehetleitner, & Müller, 2010; Schankin & Schubö, 2009; Chun & Jiang, 1998), aiming for 85% power to detect an $f(U)$ effect size of 1.0 (partial $\eta^2 = .5$, three groups, four measurements; interaction of Context (repeated, novel) \times Epoch (1–4)) with an alpha level of .05 and a nonsphericity correction of 1. All participants reported normal or corrected-to-normal vision and were randomly assigned to one of three groups (with 14 observers each): FPC rTMS, occipital rTMS, and no rTMS. The groups did not differ with regard to their mean age and sex: FPC rTMS, mean age = 26.2 years, $SD = 2.7$ years, nine women; occipital rTMS, mean age = 26.9 years, $SD = 3.8$ years, eight women; no rTMS, mean age = 26.6 years, $SD = 4.1$ years, seven women (all $ts < 0.7$, $ps > .5$). The study was approved by the ethics committee of the Department Psychology of Ludwig-Maximilians-Universität München. Observers provided written informed consent before the experiment and received €20 (~\$23.50) for their participation. All collected data is available through Open Science Framework (<https://osf.io/zhk2j/>).

Apparatus and Stimuli

The experimental routine was programmed in MATLAB with Psychtoolbox extensions (Brainard, 1997; Pelli, 1997) and was run on an Intel PC under the Windows 7 operating system. Participants were seated in a dimly lit room in front of a 23-in. LCD monitor (ASUS; refresh rate = 60 Hz, display resolution = 1920 \times 1080 pixels) at a viewing distance of 80 cm (controlled by a chin rest). The search displays consisted of 12 gray items (luminance = 1.0 cd/m²; 1 target and 11 distractors) presented against a black background (0.11 cd/m²). All stimuli extended 0.35° of visual angle in both width and height. The items were arranged on four (invisible) concentric circles around the display center (with a radius of 1.74°, 3.48°, 5.22°, and 6.96° for Circles 1 through 4, respectively). The target was always positioned on the third circle. There were overall 24 possible target locations, eight of which (two in each quadrant) were used for repeated displays with constant distractor layouts throughout the experiment. Another eight target locations (two in each quadrant) were used for nonrepeated displays with random distractor arrangements. Another set of eight additional target locations (two in each quadrant) was used for repeated displays in the test phase. The “T” target was rotated randomly by 90° either to the left or the right. The 11 remaining items were L-shaped distractors rotated randomly at orthogonal

Figure 1. Example of repeated and nonrepeated search layouts in the learning and test phases of the experiment. In repeated displays, the target position changed from learning to test, whereas the distractor arrangement remained constant. In nonrepeated displays, the target position was constant (across learning and test), but the distractor arrangement varied from trial to trial. See Methods for further details.



orientations (0° , 90° , 180° , or 270°). Figure 1 presents example display layouts.

Trial Sequence

A trial started with the presentation of a fixation cross ($0.10^\circ \times 0.10^\circ$, luminance = 1.0 cd/m^2) for 500 msec, followed by a blank interval of 200 msec, after which the search display was presented. Observers were instructed to respond as quickly and accurately as possible to the orientation of the target “T” (left vs. right). Each search display stayed on the screen until a manual response was elicited. If the “T” was rotated to the right (left), observers responded by pressing the right (left) arrow button on a computer keyboard with their right (left) index finger. Following a response error, a red minus sign appeared on screen for 1000 msec. Each trial was followed by a blank intertrial interval of 1000 msec.

Transcranial Magnetic Stimulation

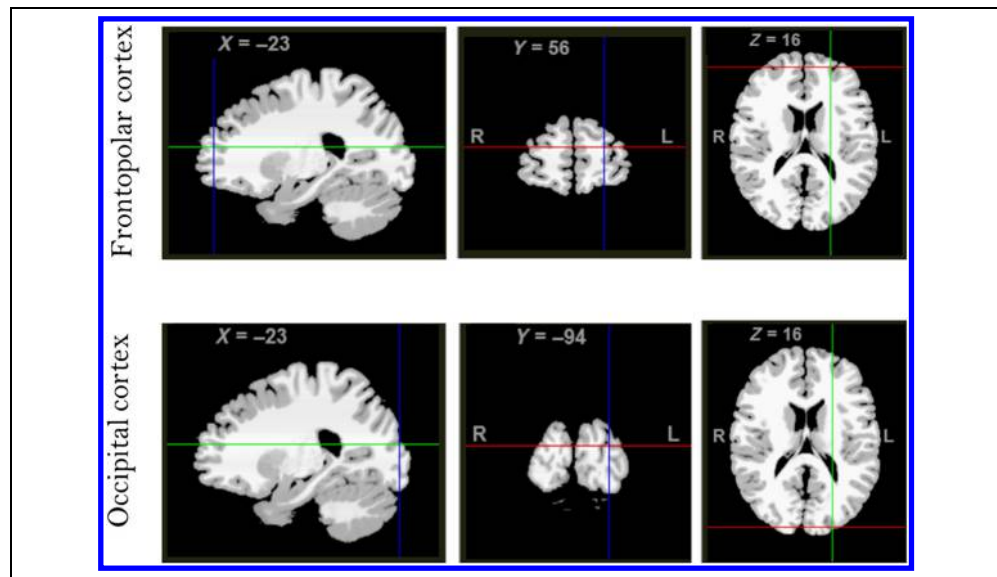
We applied rTMS (frequency = 1 Hz, intensity = 110% active motor threshold, duration = 10 min, i.e., 600 pulses) using a figure-8 coil with an internal diameter of 7.0 cm (MagPro R30 machine with MC-B70 Butterfly Coil, Magventure, Denmark). TMS was applied offline in between the two experimental phases, either to the left lateral FPC or to a control site over the occipital region. The latter condition controls for the nonspecific clicking sound and tactile sensation of TMS (Marzi et al., 1998). Coil positioning was realized by neuronavigation via frameless infrared stereotactic registration (Brainsight, Rogue Research, Canada) to determine the Montreal

Neurological Institute (MNI) coordinates of the stimulation sites based on observers’ 3T structural magnetic resonance images. We used MRI-guided TMS positioning and placed the TMS coil on the locations of the observers’ scalp corresponding to the critical cortical MNI coordinates reported by Pollmann and Manginelli (2009). For the frontopolar TMS, the MNI coordinates were $x = -23$, $y = 56$, $z = 16$, and for the occipital TMS, the coordinates were $x = -23$, $y = -94$, $z = 16$ (see Figure 2 for MNI coordinates overlaid on a reference brain image from Lacadie, Fulbright, Rajeevan, Constable, & Papademetris, 2008, using Yale BioImage Suite Package). The control occipital region was selected by preserving the x and z coordinates of the frontopolar test region while only changing the y coordinate to target occipital regions, thus ensuring that the laterality of the stimulation region was perfectly matched across the TMS stimulation conditions.

Design and Procedure

In all three groups (FPC rTMS, occipital rTMS, no rTMS), the repeated display condition comprised eight layouts associated with distinct target locations in the two phases of the experiment. For each display, target–distractor configurations were randomly generated at the beginning of the experiment. These arrangements were repeatedly presented on randomly selected trials throughout the search task, with the restriction that each repeated display was shown only once per block. Displays in the nonrepeated condition were generated online at the start of a given nonrepeated trial. In each group, a repeated arrangement was presented on half of the trials, and a

Figure 2. MRI-guided TMS positioning over frontopolar and occipital stimulation sites with corresponding MNI coordinates.



nonrepeated arrangement was presented on the other half. Trial order was randomized within each block. To equate target location repetition effects between the two types of displays, the target appeared equally often at each of 24 possible locations throughout the experiment: Eight locations were used for repeated displays, eight were used for nonrepeated displays, and the remaining eight locations were used for repeated displays after the target location change in the test phase. Furthermore, item density was controlled for each display by presenting three search items in a given quadrant (see Annac, Conci, Müller, & Geyer, 2017; Geyer et al., 2010). The orientation of the target in a given repeated display was random in each trial, whereas the orientations of the distractor elements were held constant across trials (cf. Chun & Jiang, 1998). Figure 1 depicts an example search display for the repeated and nonrepeated context conditions in the learning and test phases. The experiment was divided into two phases of 16 blocks each, yielding a total of 256 trials in each phase. Participants had the opportunity to take a short break between trial blocks or continue directly with the next block. RTs were collapsed across eight consecutive blocks to achieve reliable estimates of contextual cueing performance (cf. Chun & Jiang, 1998).

Participants in the no-rTMS group performed the visual search task without any TMS stimulation and took a 10-min break during the interval between the learning and test phases. In the TMS groups, the task structure was identical, except that participants received rTMS (1 Hz, 600 pulses, 110% active motor threshold) during the 10-min interval between the learning and test phases. There was no significant difference in mean stimulation intensity between the FPC rTMS and occipital rTMS groups, $t(27) = 1.18, p > .2$ (mean intensity =

50.1% maximal stimulator output for frontopolar group vs. 47.5% maximal stimulator output for the occipital group). Before the start of the experiment, participants performed one practice block of 24 trials (data not recorded). Observers were randomly assigned to each rTMS group/condition.

Recognition Test

At the end of the experiment, observers performed a yes–no recognition test, permitting us to assess whether they had acquired any explicit memory of the repeated configurations presented in the search task of the experiment (a “standard” procedure in contextual cueing experiments; cf. Chun & Jiang, 1998). To this end, eight repeated displays from the search task and eight newly composed displays were presented, and observers were asked to indicate whether or not they had seen a given display previously by pressing the left or the right mouse button, respectively (nonspeeded responses). The eight repeated displays, along with the eight newly generated displays, were presented in random order for four times (i.e., in four separate blocks), yielding a total of 72 recognition trials. Observers’ responses in the recognition task were nonspeeded, and no error feedback was provided.

RESULTS

For the RT analyses, error trials and “extreme” RTs below 200 msec and above 4000 msec were excluded from the data. This outlier criterion led to the removal of <3% of all trials. Mean contextual cueing effects (nonrepeated RTs – repeated RTs) and the associated differences in error rates were calculated and further submitted to a 2×2 mixed-design ANOVA with the within-group factors Experimental phase (two levels: learning, test) and Session

half (two levels: first half of a given session (=8 blocks), second half (=8 blocks). Greenhouse–Geisser corrected values are reported in case Mauchley’s test of sphericity was significant ($p < .05$). In case of significant interactions, Bonferroni-corrected pairwise t tests were used for further comparisons. Data analyses were performed with R version 3.4.3 (R Core Team, 2017).

Error Rates

We found no significant main effects or interactions for observers’ error rates in all experimental groups (all $ps > .05$). Overall, participants’ mean error rates were very low (no-rTMS group = 2.4%, FPC rTMS group = 1.3%, Occipital rTMS group = 1.9%).

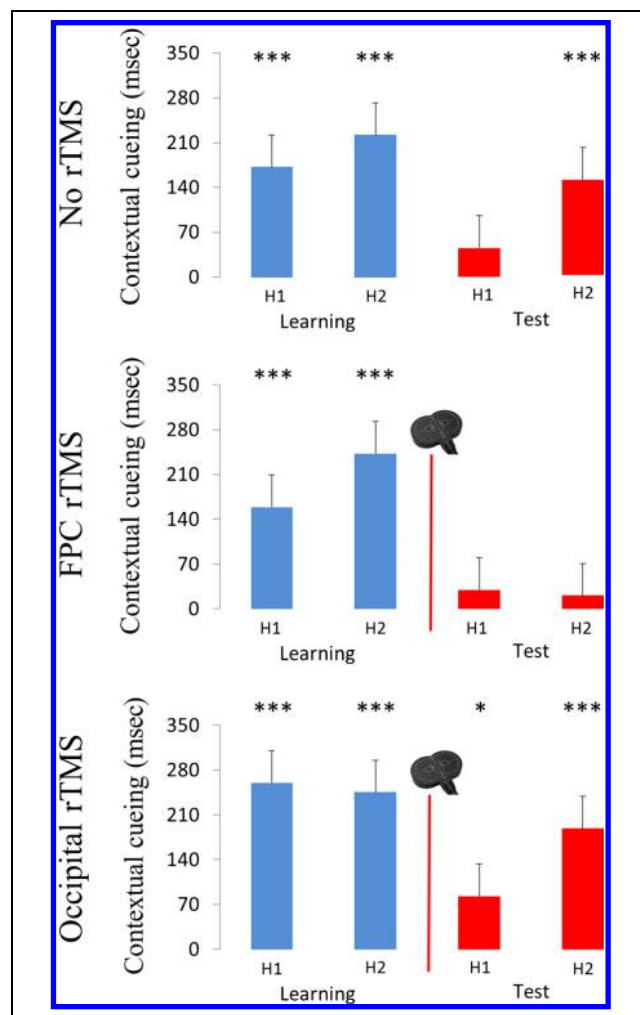


Figure 3. Mean contextual cueing effects in milliseconds [RT nonrepeated – RT repeated] and associated mean standard errors (SEM) for Halves 1 (H1) and 2 (H2) in the learning and test phases, separately for the no-rTMS, FPC rTMS, and occipital rTMS groups. The asterisks represent significance levels of * $p < .05$ and *** $p < .001$, when testing contextual cueing effects against the zero baseline.

RTs

No-rTMS Group

For the no-rTMS group (see top part of Figure 3), we (only) found a main effect of Experimental half: Across the two experimental phases, contextual cueing was overall smaller in the first half of whatever phase compared with the second half (116 msec vs. 191 msec), $F(1, 13) = 8.21$, $p = .013$, $\eta_p^2 = .39$. We also observed a marginally significant interaction of Half \times Phase, $F(1, 13) = 3.47$, $p = .085$, $\eta_p^2 = .21$: Although the cueing effect was comparable across the halves of Phase 1 (Half 1 = 188 msec vs. Half 2 = 229 msec), $F(1, 13) = 1.98$, $p = .182$, $\eta_p^2 = .13$, it was smaller in the first half relative to the second half of Phase 2 (46 msec vs. 152 msec), $F(1, 13) = 7.25$, $p = .018$, $\eta_p^2 = .36$. Note that the cueing effect was reliable (i.e., different from zero) in all halves of both the learning and test phases (all $ps < .05$, $ts > 4$), except for Half 1 of Phase 2, $t(27) = 1.11$, $p > .28$ (see also Figure 3). Next, we compared the contextual cueing effects in Half 2 of the learning phase (i.e., when the effect was firmly established immediately before target location change) to the cueing effects in Halves 1 and 2 of the test phase (thus providing measures of contextual cueing in relatively early vs. relatively late stages after the change and after some exposure to the relocated target). These comparisons revealed contextual cueing to be reduced in the first half of the test phase relative to the second half of learning phase (46 msec vs. 229 msec), $t(27) = 2.82$, $p < .01$, and then to recover again in the second half of the test phase (nonsignificant difference of 152 msec vs. 229 msec), $t(27) = 1.35$, $p = .188$. This pattern of results confirms previous findings that that cueing is compromised after target location changes but then recovers to some extent with extended experience on the relocated displays (Zellin et al., 2014).

FPC rTMS Group

In the FPC rTMS group (see middle part of Figure 3), the main effect of phase was significant: The cueing effect was overall larger in the learning phase (200 msec) than in the test phase (25 msec), $F(1, 13) = 13.23$, $p = .003$, $\eta_p^2 = .5$. In addition, we found an interaction of phase and half, $F(1, 13) = 6.6$, $p = .023$, $\eta_p^2 = .34$. Follow-up analyses for each of the two phases revealed that the main effect of half was significant in the learning phase, $F(1, 13) = 9.76$, $p = .008$, $\eta_p^2 = .43$, but not in the test phase after TMS, $F(1, 13) = 0.08$, $p = .779$, $\eta_p^2 = .01$. In the learning phase, the cueing effect was smaller in the first compared with the second half: 158 msec versus 242 msec, $t(54) = -2.08$, $p < .05$. In the test phase, by contrast, the cueing effect was markedly reduced and comparable between Halves 1 and 2: 29 vs. 21 msec ($p > .7$; neither of these effects was significantly different from zero: both $ts < 1$, $ps > .4$). Finally, the contextual cueing effect in Half 2 of the learning phase was larger

than in Halves 1 and 2 of the test phase (242 msec vs. 29 msec, $t(27) = 4.76$, $p < .001$; 242 msec vs. 21 msec, $t(27) = 4.52$, $p < .001$). This pattern indicates that TMS over the FPC effectively hinders the adaptation of contextual cueing to a changed target location within a repeated distractor layout.

Occipital rTMS Group

With rTMS of an occipital (control) region (see bottom part of Figure 3), the main effect of phase was again significant: The cueing effect was larger in the learning phase (252 msec) relative to the test phase (135 msec), $F(1, 13) = 6.58$, $p = .023$, $\eta_p^2 = .34$. The interaction of Phase \times Half was also significant, $F(1, 13) = 17.61$, $p = .001$, $\eta_p^2 = .58$. Follow-up analyses for the two phases revealed that although cueing was comparable between Halves 1 and 2 of the learning phase, $F(1, 13) = 0.2$, $p = .662$, $\eta_p^2 = .02$ (260 vs. 244 msec), the effect was smaller in Half 1 relative to Half 2 of the test phase, $F(1, 13) = 7.99$, $p = .014$, $\eta_p^2 = .38$ (83 vs. 188 msec). Of note, the cueing effect was significant in Halves 1 and 2 both in the learning and test phases (all $ps < .05$, $ts > 2.5$).

Finally, we compared the contextual cueing effects in Halves 1 and 2 of the test phase with the firmly established effect in Half 2 of the preceding learning phase: Contextual cueing was significantly reduced in the first half of the test phase (82 msec vs. 244 msec), $t(27) = 3.04$, $p < .01$, but then exhibited a reasonable (albeit nonperfect) adaptation to the changed target locations—in the second half (188 msec vs. 244 msec), $t(27) = 1.18$, $p > .2$. Thus, the results of the occipital rTMS group mirror those of the “baseline” no-rTMS group (in which participants had not received any intervention at all).

Omnibus Analysis

To further test and directly compare the effect patterns among the three groups, we entered the mean contextual cueing effects into a $3 \times 2 \times 2$ mixed-design ANOVA with the between-subject factor rTMS group (three levels: no rTMS, FPC rTMS, occipital rTMS) and the within-subject factors Phase (two levels: learning, test) and Half (two levels: first half, second half). This ANOVA revealed a significant main effect of Phase: cueing was overall reduced after the target location changes in the test phase relative to initial learning phase (87 msec vs. 216), $F(1, 39) = 20.16$, $p < .001$, $\eta_p^2 = .34$. The main effect of Half was also significant: Cueing was overall more marked in the second half relative to the first half of whatever phase (179 msec vs. 124 msec), $F(1, 39) = 11.29$, $p = .002$, $\eta_p^2 = .22$, of each session. Furthermore and most importantly, the three-way interaction was significant, $F(2, 39) = 10.02$, $p < .001$, $\eta_p^2 = .34$. As can be seen from Figure 3, contextual cueing was overall comparable among the three groups in the initial

learning phase, and it was substantially reduced immediately after the introduction of the target location change in the test phase (compare Half 2 of the learning phase with Half 1 of the test phase) for all groups. The significant three-way interaction then arises from the fact that a recovery of contextual cueing, indicative of successful adaptation to the target location change, in Half 2 of the test phase was evident only for the no-rTMS (“baseline”) and occipital rTMS (“control”) groups, whereas there was no indication of a recovery—or relearning of the changed target location—whatsoever in the FPC rTMS group.¹ This result was supported by an additional series of correlation analyses that tested whether the strength of contextual cueing before relocation (in the learning phase) was related to the degree of adaptation (or the lack of it) after the target location change in the test phase. None of these correlations were significant (no-rTMS group: $r = -.01$, $t(54) = -0.09$, $p > .9$; FPC rTMS group: $r = .19$, $t(54) = 1.44$, $p > 1.5$; occipital rTMS group: $r = .06$, $t(54) = 0.46$, $p > .6$), indicating that variations in contextual cueing that emerged in the test phase are causally related to the specific TMS condition (rather than the magnitude of cueing in initial learning).

Recognition Test Performance

Explicit recognition performance was analyzed by comparing observers’ hit rates (repeated display correctly judged as repeated in the recognition test) with their corresponding false alarm rates (nonrepeated display incorrectly judged as repeated) by means of a 2 (Type of response: hit, false alarm; within-subject variable) \times 3 (Group: no rTMS, FPC rTMS, occipital rTMS; between-subject variable) mixed-design ANOVA. On average, observers correctly recognized repeated displays in 51% of the trials (hit rate), whereas they falsely classified nonrepeated displays as repeated in 48% of trials (false alarm rate). This hit rate was not significantly different from the false alarm rate, $F(1, 39) = 1.75$, $p > .19$, $\eta_p^2 = .043$, and there was also no difference across the three groups (interaction of Group \times Response Type: $F(2, 39) = 2.5$, $p > .09$, $\eta_p^2 = .114$). The main effect of Group was also not significant, $F(2, 39) = 1.45$, $p > .2$, $\eta_p^2 = .067$. This suggests that observers could not explicitly recognize repeated display arrangements.

DISCUSSION

Objects in our visual environment typically appear in a certain context that remains invariant across repeated encounters (e.g., a mail box in the front yard; see Brady, Konkle, Oliva, & Alvarez, 2009; Palmer, 1975). Our visual system has the capability to extract and learn such context–object associations, which in turn facilitate processing of task critical target objects. In recent years, numerous studies have shown that visual search can

substantially benefit from learned distractor-to-target spatial relations (see Goujon, Didierjean, & Thorpe, 2015; Wolfe & Horowitz, 2017, for reviews). However, statistical context learning should also exhibit a degree of flexibility to incorporate changes that may occur in our sensory environment. Specifically, context memory should be able to adapt to target position changes, ensuring that attention is effectively allocated to targets at their novel locations, rather than prioritizing no longer relevant positions in the environment. In a recent fMRI investigation, Pollmann and Manginelli (2009) suggested that FPC may play an important role in this type of context adaptation. Specifically, they suggested that FPC detects discrepancies between the current sensory input and associated context-based expectations and then informs other (frontoparietal) attention structures about these inconsistencies, which could eventually lead to a shift of visuospatial attention to the changed target position (“FPC+” hypothesis). Although such a facilitatory FPC influence may eventually lead to context adaptation, a number of studies have reported rather inefficient, slow, and resource-demanding adaptation to changed distractor-to-target spatial relations (Annac et al., 2017; Zellin et al., 2013, 2014). Based on these findings, this study was designed to test an alternative account of FPC functions in context adaptation, namely, that FPC contributes to the regulation of prediction errors by “explaining away,” that is, suppressing the changed target position and thus effectively supporting already acquired contextual memory representations (FPC– hypothesis). We hypothesized that if FPC facilitates the processing of changed target locations (FPC+), then interference with FPC by means of TMS would weaken context adaptation even further, as there would be no guidance from FPC on the reallocation of attention after target position changes. Alternatively, if FPC supports attention guidance by previously established context memories (FPC–), then we would expect to find improved adaptation, because attentional (mis)guidance would be reduced during to the inactivation of this region. The results clearly support the “FPC+” hypothesis. Stimulation of FPC in-between a learning phase and a test phase did not yield any context adaptation. This is in contrast with the no-TMS and occipital rTMS conditions, in which there was a relatively high degree of adaptation, approaching (though, within the time on task allowed, not quite reaching) the level of the initial learning effect.

Our findings provide important novel insights into the role of the FPC: They affirm a causal involvement of the left FPC in the adaptation of learned target–distractor arrays and thus in statistical context (re)learning in visual search. Pollmann and Manginelli (2009) used fMRI to show that neural activity in the left FPC increases selectively after target location changes in repeated displays. They hypothesized that these activations arise because FPC signals a perceptual change to frontoparietal brain areas, providing the basis for these attention-guiding

networks to adapt to the change and to update context memory. The current study provides a causal test of this hypothesis. Participants were unable to adapt their context memory, even after hundreds of repetitions, when normal FPC functioning was disrupted, that is, frontopolar TMS hinders context adaptation.

Other studies lend further support to his account of FPC function. For instance, Badre and Wagner (2005) studied the role of FPC in proactive interference, that is, when a memory relating to a past experience hinders the subsequent acquisition of new memories. Participants in their study were asked to maintain a set of target words and indicate whether a subsequently presented “probe” word was from the target set. Badre and Wagner found that probe words not included in the current target set but included in the target set on the preceding trial resulted in impaired performance and in increased activation in the left FPC—suggesting that the FPC is involved in the resolution of proactive interference when information that was previously held in memory interferes with performance on the current trial. In a different study, Badre and D’Esposito (2007) further examined the involvement of the left FPC in a varied/competing mapping task. Participants’ task was to compare two test items in terms of one of four dimensions (texture, orientation, shape, or size), that is, they had to make a decision whether the two items were the same or different in terms of the relevant dimension—which was cued on each trial by the color of a square frame around the test items (at the start of a trial). Crucially, Badre and D’Esposito (2007) varied the mapping between a given colored square and a given dimension. In the consistent condition, a given context color did reliably indicate a single response dimension across all trials/blocks. In the inconsistent condition, by contrast, the assignment of a given context color to a response dimension was variable across blocks (e.g., in some blocks, a green frame meant that observers had to compare the two test items in terms of their shape [while ignoring their other properties], whereas in other blocks it meant they had to compare the texture of the test items), thus engendering some competition between the color-to-dimension mappings. Badre and D’Esposito (2007) found increased activation of the left FPC in the inconsistent condition, when a color cue was predictive of multiple target dimensions on different blocks. This indicates that the FPC was involved in the resolution or reorganization of cue–response associations in the inconsistent mapping task. The current data are in line with such an interpretation: The left anterior FPC might also be involved in the detection of changed target–distractor spatial associations and their corresponding reorganization, that is, adaptation, in a visual search statistical learning task.

The present findings may also indicate that the FPC is responsible for the acquisition of rules and environmental regularities irrespective of previously established

memories. For instance, previous observations showed that rTMS over the left (Costa et al., 2011) and right (Costa et al., 2013) FPCs led to impaired visual-spatial prospective memories. Because contextual cueing requires the detection of repeated target-distractor arrays, the FPC may be involved in the detection and subsequent acquisition of such associations. In line with this idea, Strange, Henson, Friston, and Dolan (2001) used fMRI to show that the bilateral FPC mediates the learning of rules: They observed increased activation in the bilateral FPC when a new rule had to be learned, and this activation decreased with improving task performance, possibly representing rule acquisition. Recently, Paniukov and Davis (2018) showed that the FPC continues to integrate information about rules of a given task even after the correct rule was extracted. This indicates that FPC is involved in a constant monitoring of evidence to support rule-based representations. Seger and Cincotta (2006) and Liu, Braunlich, Wehe, and Seger (2015) found that the FPC was more active during rule learning compared with rule application in variants of a classification task. Based on this, it was suggested that FPC may be involved in the acquisition and maintenance of rule-based learning. Crucially, this account may be in line with the findings of Pollmann and Manginelli (2009) that FPC activations were lower for repeated relative to nonrepeated arrays during initial context learning and higher after target relocation. Specifically, once a given spatial regularity is learned, activity in the FPC is reduced (though not completely gone; see Paniukov & Davis, 2018), but it is increased again after target is relocated and new associations have to be acquired (Strange et al., 2001).

Thus, FPC appears to be involved not only in the relearning after a target location change but also in initial learning of target-distractor constellations, before any target location changes. For instance, stimulation of the FPC may interfere with the efficient use of contextual cues, as disruption of the FPC may result in an inability or difficulty to acquire spatial target-distractor associations. This prediction receives some support from the findings of Nydam, Sewell, and Dux (2018), who applied cathodal transcranial direct current stimulation over the left pFC while participants performed a standard contextual cueing task—which resulted in a reduction of contextual cueing during the first half of experiment. Similar results have been obtained with other perceptual decision tasks, including visual search (e.g., Raja Beharelle, Polanía, Hare, & Ruff, 2015; Reinhart & Woodman, 2015). Interestingly, using anodal transcranial direct current stimulation over the FPC, these studies found an increased proportion of responses toward novel, that is, unlearned, stimuli (Raja Beharelle et al., 2015) or improved learning of the target's perceptual attributes in the context of a visual search task (Reinhart & Woodman, 2015). Overall, this work points to a functional role of FPC in setting up context-based

memories that, once established, require maintaining the balance between acquired memories and the currently available stimulus information. Assuming the ubiquity of statistical learning, this would be equivalent to an adaptation of existing context memories with regard to the new stimulus characteristics. In this view, FPC would modulate both initial context learning and later context adaptation.

Conclusion

Several previous visual search studies (Pollmann et al., 2006, 2007; Weidner et al., 2002; Pollmann, Weidner, Müller, & von Cramon, 2000) have shown that the left FPC shows transient signal increases when the target's defining perceptual dimension changes across successive trials. These activation increments were interpreted as enhanced requirements for attention to shift to the target dimension, thus requiring an up-modulation of salience signals, which represent the conspicuity of the target in relation to the surrounding distractor items. Our results extend these previous findings by showing that the FPC is not only sensitive to the repetition of certain target dimensions (color, orientation, etc.) but also monitors the spatial array of learned, invariant search layouts within which the target is embedded. Although we have not measured visuospatial attention directly, the present finding would generally support the view that the detection of changes in previously learned search layouts leads to an FPC biasing signal to guide attention more efficiently toward the changed target location in an attempt to overcome the detrimental effects resulting from previously learned context representations.

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Reprint requests should be sent to Artyom Zinchenko, Department Psychologie, Lehrstuhl für Allgemeine und Experimentelle Psychologie, Ludwig-Maximilians-Universität München, Leopoldstraße 13 80802 München, Germany, or via e-mail: artyom.zinchenko@psy.lmu.de.

Note

1. Note that three further comparisons, that is, Experiment \times Phase \times Half mixed-design ANOVAs, comparing each experimental condition with each of the other conditions, revealed a significant three-way interaction of experiment, phase, and half in the analysis of the FPC rTMS and occipital rTMS groups, $F(1, 26) = 21.4, p < .001, \eta_p^2 = .45$, as well as the FPC rTMS and no-rTMS groups, $F(1, 26) = 9.86, p = .004, \eta_p^2 = .27$. By contrast, the three-way interaction was nonsignificant in the occipital rTMS and no-rTMS groups, $F(1, 26) = 1.49, p = .233, \eta_p^2 = .05$.

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